

UNIVERSITY OF  
**ROCHESTER**  
MEDICAL CENTER

CANCER CENTER  
IMMUNOLOGY DIVISION

September 1, 1993

Dr. Vincent Lisanti  
The Council for Tobacco Research-USA, Inc.  
900 Third Avenue  
New York, NY 10022

Dear Dr. Lisanti:

*Send Instructions  
for Preliminary  
application*

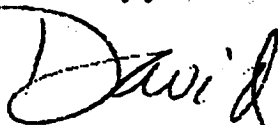
As you know, several research projects in my laboratory had been supported by the Council for Tobacco Research over the last several years. This support led to funding by the American Cancer Society and the NIH. Our research efforts have now expanded into additional areas and led to the development of new proposals, for which we seek funding. I am writing to familiarize you with these two projects in order to ascertain whether the Council for Tobacco Research would entertain a proposal to support one of these projects.

The first project evolved from our analysis of murine B lymphoma growth, initially supported by the CTR, and involves the examination of the roles played by oncogenes and anti-oncogenes in human B-lymphoma cell regulation. Indeed, we hope to eventually apply this knowledge to assess the prognostic value receptor-mediated induction of oncogene and anti-oncogene effects in human lymphomagenesis. Specifically, our goals are to evaluate the post-translational modification of the retinoblastoma gene product, a cell cycle controlling element, and the modulation of the *myc* oncogene in the regulation of cell cycle progression and the induction of apoptosis. Based on evidence we have accumulated in murine models, and preliminary data with human lymphoma cells, we believe it is an appropriate time to expand our project in this new direction.

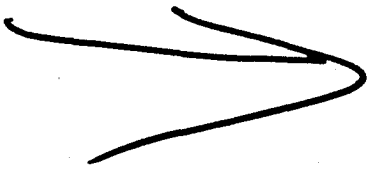
A second project involves the development of novel fusion proteins and their expression both in retroviral vectors in bone marrow cells or in transgenic mouse lines. A preliminary version of this grant proposal was submitted to the CTR a year ago, at which time you suggested that a delay in re-application would be appropriate. We now have established transgenic mice and have prepared retroviral vectors for the expression of a unique epitope either as a free peptide or as part of an IgG fusion protein. Our data so far suggest that the latter fusion protein is tolerogenic for B cells, whereas the peptide is capable of inducing tolerance in T cells, but not in B cells. This differential tolerance provides us with a model system to examine unresponsiveness in different populations to the same epitope and apply this knowledge to the modulation of human autoimmune diseases.

I hope these brief overviews provide you with sufficient information to evaluate the prospects for submitting a new proposal to the Council for Tobacco Research. I appreciate your consideration and past support.

Sincerely yours,



David W. Scott, Ph.D.  
Immunology and Immunotherapy Division  
Dean's Professor of Immunology



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